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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/384,379	08/27/1999	YOSUKE AOKI	2167-0110P	7722

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EXAMINER
NGUYEN, BAO THUY L

ART UNIT	PAPER NUMBER
1641	12

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/384,379	Applicant(s) AOKI ET AL	
	Examiner Bao-Thuy L. Nguyen	Art Unit 1641	

-- Th MAILING DATE of this communication appears on the cov r sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 15, 2002 has been entered.

2. Claims 1-4 have been canceled. Claims 6-9 have been added. Claims 5-9 are pending.

3. The text of those US codes not found in this office action may be found in a previous office action.

Claim Rejections - 35 USC §103

4. Claims 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al (Clinica Chimica Acta, 178:193-209, 1988) in view of Kohler (Science, 233:1281-1286, 1986).

Aoki discloses an enzyme immunoassay for determining human medullasin in peripheral blood. Aoki discloses beads coated with IgG obtained from immunized rabbits incubated with medullasin, Fab'-peroxidase conjugate was added, and peroxidase activity bound to the beads was measured by a fluorophotometer. Aoki discloses the determination of multiple sclerosis (MS) by detecting medullasin activity in granulocytes. See pages 194-196.

Aoki differs from the instant invention in failing to teach the use of a monoclonal antibody to medullasin.

Kohler, however, discloses a method for producing hybridoma cell lines secreting monoclonal antibodies using lymphocyte fusion techniques. Kohler discloses that polyclonal

antibodies suffers from major disadvantages such as low titers, heterogeneous, limited supply and impossible to reproduce the same combination of specific antibodies in a new animal. In contrast, lymphocyte fusion provides the advantages of specificity, unlimited supply of antibody. The use of impure antigens still leads to pure antibody reagent. All specificities can be rescued. Enrichment or specific hybridomas is possible. A high level of antibody secretion is observed. The hybridoma cell lines can be manipulated to produce antibodies not found in nature, and the method is generic such that antibodies against any antigen may be produced. See page 1281.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a monoclonal antibody against the human medullasin of Aoki using the method taught by Kohler because Kohler teaches that any substance that can elicit a humoral response can be used to prepare monoclonal antibodies. Kohler further teaches that monoclonal antibodies provide advantages not found with polyclonal antibodies. These advantages include specificity of binding, homogeneity, and ability to be produced in unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique and chosen specificity. Because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. In addition, one unique advantage of hybridoma production is that impure antigens can be used to produce specific antibodies. A skilled artisan would have had a reasonable expectation of success and would have been motivated to use the techniques of Kohler to produce monoclonal antibodies to human medullasin for use in an assay to detect medullasin such as taught by Aoki.

Response to Arguments

5. Applicant's argument filed October 15, 2002 has been fully considered but is not deemed to be persuasive.

Applicant argues that the office action fails to show that one of ordinary skill in the art would be motivated to combine the teachings of Aoki with Kohler to arrive at an immunoassay that is capable of producing results within one hour, and that uses monoclonal antibodies. Applicant argues that Aoki uses a polyclonal antibody in it's assay and that the method disclosed takes as long at 18 hours to complete, as oppose to the instant invention where only 1-hour is required. Applicant argues that Aoki fails to disclose or suggest shortening the incubation times for arriving at the present invention. Applicant also argues that the monoclonal of the instant invention possess high reactivity and can determine medullasin content in a very short time.

These arguments have been fully considered but are not deemed to be persuasive. The office action clearly states the motivation and means for making and using monoclonal antibodies in an immunoassay for human medullasin. The Aoki reference clearly teaches the usefulness of medullasin in both diagnosing and evaluating MS. And, Kohler clearly teaches that it is both conventional and advantageous to make and use monoclonal antibodies for their well-recognized advantages. Therefore, one of ordinary skill in the art, in looking for a more sensitive assay to detect medullasin, would have been motivated to make and use monoclonal antibodies that specifically recognizes and binds to human medullasin. As evidence in Hybritech Incorporated v. Monoclonal Antibodies, Inc. CAFC 231 USPQ 81 (9/19/1986), the principle for the production of monoclonal antibodies is so well known in the art that it is a

routine matter. Furthermore, monoclonal antibodies have been recognized as providing advantages that are not present in polyclonal antibodies, therefore, there is clearly a showing of a reasonable expectation of success as well as motivation, and one of ordinary skill in the art would have been motivated to use the techniques of Kohler to produce monoclonal antibodies to a well known protein, such as human medullasin. Furthermore, it is well recognize and is conventional in the art to elicit antibodies to isolated proteins for a variety of uses as taught by Aoki and Kohler, and one of ordinary skill in the art would have had an extremely reasonable expectation of success in achieving the expected result, i.e. generating monoclonal antibodies, specifically reactive with a known protein, medullasin for use in immunoassay to detect the protein. It would have been obvious to have generated monoclonal antibodies in order to provide a potentially unlimited source of homogeneous reagent for clinical studies of the protein such as taught by Aoki.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the shortened time of the immunoassay) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The instant claims are directed to a generic immunoassay to detect medullasin using monoclonal antibodies, such an assay is obvious over the prior art of record.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (703) 308-4243. The examiner can normally be reached on Monday, Wednesday and Thursday from 9:00 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
February 11, 2003